

**I. Remarks**

After entry of the amendment, claims 6-25 are pending.

The Related Applications section has been edited.

Claims 1-5 have been canceled without prejudice and replaced with claims 6-25, which comply with the restriction requirement, and which are supported by the originally filed claims and specification. Applicants reserve the right to file divisional applications directed to the non-elected subject matter.

No issues of new matter should arise and entry of the amendment is respectfully requested.

**A. Restriction Requirement**

In response to the Restriction Requirement of January 13, 2005, Applicants elected Group 45, with traverse. In the Office Action dated May 4, 2005, the Examiner made the restriction requirement final. Applicants thank the Examiner for considering and adopting Applicants proposed restriction requirement for Group B.

**B. Rejection under 35 U.S.C. § 103**

Claims 1-3 and 5 are rejected under 35 U.S.C. §103(a) as being obvious over Sandrock et al (U.S. Patent No. 5,428,061) in view of either Lundy et al (U.S. Application No. 2001/001285) or Smith et al (U.S. Patent No. 5,691,423).

Applicants respectfully traverse the rejection and respectfully submit that the presently claimed invention is unobvious over the cited references.

Sandrock discloses the use of cysteine-containing nitrate compounds for the treatment of cardiac diseases. The Examiner admits that Sandrock does not disclose the use of the cysteine-containing nitrate compounds for the treatment of gastrointestinal disorders. There is nothing in Sandrock to motivate one to use cysteine-containing nitrate compounds for the treatment of gastrointestinal disorders. Sandrock is non-analogous art that describes methods of use that are unrelated to the claimed invention.

Lundy and Smith do not cure the deficiencies of Sandrock.

Lundy discloses the use of nitric oxide oxindole prodrugs for the treatment of pain, inflammation, fever, gastrointestinal lesions and gastrointestinal problems caused by COX-2 inhibitors and NSAIDs.

The compounds of the invention are not disclosed in Lundy, and the compounds of the invention are structurally unrelated to the compounds described in Lundy. The only commonality between the compounds disclosed in Lundy and the compounds of the invention is that they contain at least one sulfur atom. One skilled in the art would readily appreciate that there are infinite numbers of compounds that contain at least one sulfur atom and that the compounds disclosed in Lundy and the compounds claimed in the present invention are totally unrelated and structurally different. Accordingly, the teachings in Lundy do not disclose or suggest the use of the presently claimed sulfur containing compounds for the treatment of gastrointestinal disorders.

Additionally, Lundy does not provide any motivation for one skilled in the art to use the claimed compounds for treating gastrointestinal disorders. Accordingly, the teachings in Lundy do not disclose or suggest the use of the presently claimed sulfur containing compounds for the treatment of gastrointestinal disorders.

Smith discloses the use of polysaccharides containing a nitric oxide-releasing  $N_2O_2$ -functional group bound to a polymer for treating biological disorders. The polysaccharides containing a nitric oxide-releasing  $N_2O_2$ -functional group disclosed in Smith are structurally different from the nitric oxide donating compounds claimed in the present invention.

Accordingly, the teachings in Smith do not disclose or suggest the use of the presently claimed sulfur containing compounds for the treatment of gastrointestinal disorders.

Smith suggests that nitric oxide is implicated in “gastric motility, neurotransmission, nociception and other roles.” Applicants respectfully submit that the presently claimed methods are unrelated to “gastric motility” (i.e., movement), neurotransmission, and nociception, and that Smith does not provide any motivation or suggestion to (i) treat and/or prevent gastrointestinal disorders; (ii) treat and/or improve gastrointestinal properties of COX-2 selective inhibitors; (iii) decrease the recurrence of ulcers; (iv) improve the gastroprotective properties, anti-*Helicobacter pylori* properties or antacid properties of proton pump inhibitors; or (v) improve the

gastroprotective properties of H<sub>2</sub> receptor antagonists with nitric oxide donor compounds.

Moreover, there is no evidence of record of any relationship between Smith's methods of gastric motility, neurotransmission, nociception and the claimed methods of treating gastrointestinal disorders. Thus, Smith is non-analogous art. In view thereof, Applicants respectfully submit that Smith cannot render the presently claimed methods obvious.

Lundy and Smith do not disclose or suggest any compounds that are structurally similar to the claimed compounds of the present invention. Sandrock and Smith do not disclose or suggest any methods that are related to the claimed methods of the present invention.

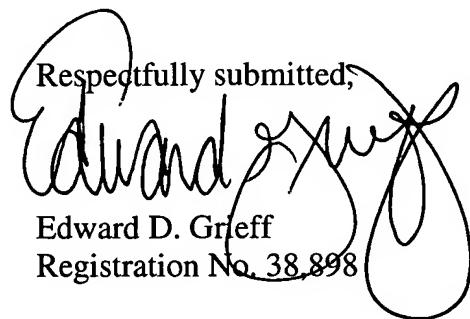
Again, Lundy and Smith do not cure the deficiencies of Sandrock. Lundy does not provide any motivation or suggestion to modify Sandrock to arrive at the claimed invention. Smith does not disclose the currently claimed methods. In view thereof, the combination of Sandrock, Lundy and Smith do not disclose suggest or motivate one to use a cysteine-containing nitrate compound for the treatment of gastrointestinal disorders.

Applicants respectfully submit that the claims of the present invention are unobvious over the cited references, alone or in combination, and respectfully request the rejection under 35 U.S.C. § 103(a) be withdrawn.

The Office Action mentions Siegfried; however, Siegfried does not form the basis of the § 103 rejection. Siegfried discloses the use of cysteine-containing nitrate compounds for the treatment of cardiac diseases. Siegfried does not disclose the use of the cysteine-containing nitrate compounds for the treatment of gastrointestinal disorders. There is nothing in Siegfried to motivate one to use cysteine-containing nitrate compounds for the treatment of gastrointestinal disorders. Moreover, Siegfried does not cure the deficiencies of Smith. Neither Smith nor Siegfried disclose the currently claimed methods. Hence, Smith in combination with Siegfried does not provide any motivation for one skilled in the art to arrive at the methods of the presently claimed invention.

**C. Conclusion**

Applicants respectfully request reconsideration and allowance of claims 6-25. Examiner Audet is encouraged to contact the undersigned at 202-942-8453 concerning any questions about the application.

Respectfully submitted,  
  
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